REMARKS

Revocation and New Power of Attorney & Change of Correspondence Address

Revocation of Powers of Attorney with New Powers of Attorney and Change of Correspondence Address Forms signed by the Applicants Sudhir Paul and Yasuhiro Nishiyama appointing the undersigned to prosecute the above-referenced patent application before the U.S. Patent and Trademark Office have been submitted and accepted.

Status of the claims

Claims 1-61 are pending and subject to restriction. Claims 1-5, 19, 21-22, 25-26, 28, and 44-45 are amended herein. Claims 6-9, 23-24, 29, 35-43, and 49-61 are canceled. New claims 62-65 are added. No new matter is added in any amendment.

Claim amendments

Claim 1 is amended to delete the phrase "selected from the group consisting of an amino acid residue, a sugar residue, a fatty acid residue and a nucleotide" since claim 1 does not restrict the components of the L1...Lx...Lm ligand determinant. Also, claim 1 is amended to insert the conjunctive "and" before the last claim element. Claims 6-9 and 23-24 are canceled. Independent claims 25 and 44 are amended to depend from amended independent claim 1 and independent claim 28 is amended to depend from amended claim 25. Claim 29 is canceled as redundant to claim 26 since claim 28 now depends from claim 25.

Claims 2-5 and 21-22 are amended to correct antecedency of the preambles to recite "The CAL" as these are dependent claims. Claim 3 also is amended to recite a functional group of "an amino acid residue" since L" is a functional group of a single component unit L_x in this instance would be an amino acid. Claims 21-22 also are amended to recite that the ligand determinant . . . . $[L_1 \ldots L_x \ldots L_m]$ . . . is a "polypeptide comprising" a linear or a non-linear polyamino acid, respectively.

Claims 19, 26 and 45 are amended to delete the phrase "and m is 4 to 22" and to thus properly add the conjunctive "and" after the claim element "R_1 is an oxygen or sulfur atom". Claim 1 recites that m is 1 to 30 and claims 19, 26 and 45 depend directly or indirectly from amended independent claim 1. Also, claims 26 and 46 are amended to add the omitted term "side" before chain, as in original claim 3.

New claims 62 and 64 limit the L_1 and L_m components of the ligand determinant to polypeptides, polysaccharides, lipidic groups, or nucleic acid groups and Lx is limited to an

amino acid residue, sugar residue, a lipid residue, or a nucleotide as originally recited in independent claim 1 (pg. 19, ll. 28 to pg. 20, ll. 6). As such, new claim 63 further limits L_1 and L_m to polypeptide components and Lx is an amino acid (see claims 20-21). New claim 65 further limits the L' functional group of Lx to side chains of the twenty amino acids recited in amended claim 26.

Non-elected claims 35-43 and 49-61 are canceled. Group I claim 50 should properly depend from independent claim 49 and thus is canceled as a non-elected claim.

Election/Restrictions

Applicants have added new claims 62-65 to depend directly or indirectly from amended independent claim 1 and also amended independent claims 25, 28 and 44 to depend directly or indirectly therefrom, as discussed supra and canceled Group 1 claims 5-9, 23-24, 29, and 50. The Applicants hereby elect the remaining Group I claims 1-4, 10-22, 25-34, and 44-48, drawn to a covalently reactive ligand analogue (CAL) of formula I, methods of making CAL and methods of activating or inactivating a nucleophilic receptor (NuR), without traverse. Applicants submit that new claims 62-65 properly belong in Group I and should be included in the election without traverse.

As such, Applicants make the following species elections for a CAL without traverse.

1) L_1 and L_m are polypeptides and L_x is an amino acid.

2) n is 1. Applicants wish to state that a CAL with one subunit, i.e., n is 1, is not patentably distinct from any other n value up to and including the recited n is 1000. What is patentably distinct is the CAL structure as shown within the brackets, not how many individual CALs are linked together.

3) Y' is (4-amidinophenyl)methylamine.

Applicants make the following species elections for a CAL with traverse.

1) m is 1 to 30. The specification discloses CALs where the ligand determinant is composed of, *inter alia*, HIV-1 gp120 residues 421-436, 421-432 and 426-431 which are overlapping sequences contained within gp 120 421-436 and a 28 residue VIP-CAL peptide. Applicants submit that, given the species election of L_1 and L_m as polypeptides and L_x an amino acid, searching an amino acid ligand determinant where m is 1-30 residues would not constitute an undue burden and respectfully request that the Examiner make such a search.

2) L' is carboxyl group. As an amino acid L1...Lx...Lm ligand determinant is elected as a species, L' therefore is a functional group of an amino acid, i.e., NH_2 or COOH as terminal residue groups or terminal sidechain groups and SH or OH sidechain groups. As discussed *infra*, Applicants provisionally elected a Y" species of forming an amide bond with Lx. Since an amide bond is a covalent bond between an amino and carboxyl group, Applicants respectfully request that the amino group species for L' be rejoined with the carboxyl L' group. A search of the CAL would entail searching for an amide bond linking the Y group and not the separate amino and carboxyl functionalities and would not constitute an undue burden.

3) Y" forms an amide bond with L' and Y'. Applicants provisionally elected carboxyl as L' and requested rejoinder with L' as an amino group. As such, Applicants also request that Y" as a suberoyl group be rejoined with Y" as an amide bond. The dicarboxy functional groups in suberic acid form amide bonds with both the amino groups of L' and Y' (4-aminophenyl)methylamine.

4) Y is phosphonate diphenylester group. One or both phosphinic hydroxyls may be substituted with the same or different substituents. Applicants submit that rejoining phosphonate monophenylester with the phosphonate diphenylester would not place an undue search burden on the Examiner

Also, generally, Applicants wish to respond to the Examiner's reasoning for lack of unity of invention. Applicants have amended independent claim 1 to recite that L_x is a component unit of the ligand determinant (which is L1...Lx...Lm) and have amended independent claims 25, 28 and 44 to depend from amended independent claim 1.

First, the Examiner states that Taguchi *et al.* teaches the synthesis of the conjugate (page 3168) and, thus, the technical feature is not a contribution over the art and the claims lack unity. Formula (1) of Claim 1 defines compounds that are chemically different from the conjugate described by Taguchi *et al.* Thus, the prior art synthesis objection does not apply. For example, the electrophile in the present invention is located on the side chains of macromolecular units Lx. Taguchi *et al.* teaches only electrophilic groups connected to the macromolecular backbone, a feature that restricts accessibility and flexibility. This is an important difference, as the side chain location and inclusion of linkers enhances the flexibility and accessibility of the electrophiles, thereby ensuring a more a rapid reaction with NuRs. This is a novel feature not contemplated by Taguchi *et al.* Another example difference is that in claim 1, the electrophilic group is flanked on both sides by the component determinants of the macromolecule in the present invention. This increases the noncovalent binding affinity of the

CALs. Taguchi *et al.* teaches electrophiles that have macromolecular determinants only on one flank, restricting the strength of noncovalent binding.

The Examiner states that the compounds fail to satisfy requirement (A) (common technical feature) as they are expected to either activate or inactivate NuR, and thus do not have the same activity/function because they are expected to do contrary activities. The differing biological consequences do not compromise the inventive unity derived from the common concept, that is, the occurrence of covalent NuR binding guided by noncovalent binding. A CAL can work as an agonist or antagonist for the same NuR expressed in different types of cells, because the signal transduction machineries in different cells are divergent. The recitation of "activate or inactivate" or "agonism or antagonism" is in the preambles of the claims and recite commonly known ways to affect a nucleophilic receptor on a cell surface. What is common and unifying is that the CALs of amended independent claim are used to contact a nucleophilic receptor that reacts specifically with the ligand determinant of the CAL

The Examiner states that the claim recites no structure, thus failing to meet the requirements of(B)(I). Applicants are assuming the Examiner means no common structure. As amended, independent claim 1 now recites a common CAL structure.

The Examiner states that one of skill in the art would not recognize these divergent compounds, or other compounds asserted to have said activity/function, as required, to function in the context of the instantly claimed invention and, thus, the claim fails to meet the requirement of (B)(2). As discussed supra, ALL of the CAL structures covered by Formula (1) of amended Claim 1 share the common feature of covalent binding to NuRs guided by noncovalent binding thereto to elicit an affect on the NuR. One skilled in the art is quite aware that all receptor-ligand binding interactions in nature occur by noncovalent means (this is text-book knowledge). The diversity of structures contained in the present invention simply mirrors the diversity of ligands found in nature. Therefore, one skilled in the art will readily appreciate that the divergent compounds claimed as CALs will be useful for the same purpose, i.e., covalent binding to NuRs guided by noncovalent binding.

The Examiner states that claims 1-61 are generic to an infinite number of compounds encompassed by formula (I). Applicants submit that claim 1 may encompass a large number of compounds, but not an infinite number. As discussed supra, Lm is limited to 30 and a single CAL unit where n is 1 is not patentably distinct from one where n is 1000. Lx is also a limited number of functional groups determined by the ligand determinant. Placement of the same electrophiles at differing positions within a CAL macromolecular determinant

increases the number of compounds further, but this number is still within the range of modern macromolecular screening methods.

Applicants submit that the provisionally elected species of CAL reads on claims 1-4, 11, 13-15, 18-19, 21-22, 25, 27-28, 44, 46-47, and 62-65, as amended herein. Should the Examiner rejoin the requested species, the rejoined CAL species would also read on claims 10, 26 and 45.

This is intended to be a complete response to the Restriction Requirement mailed March 10, 2009. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution. Applicants enclose a Petition for a One Month Extension of Time. Please charge the $65 petition fee under 37 C.F.R. 1.17(a) to the credit card identified on the attached Form PTO-2038. **Only in the absence** of Form PTO-2038, please debit any applicable fees from Deposit Acct. No. 07-1185 upon which the undersigned is allowed to draw.

Respectfully submitted,

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